REMARKS

Claims 1-16 are pending in the present application. Claims 1 and 8 have been amended to clarify that the phrase "effective amount" refers to an amount effective to activate NK cells. Claim 8 has also been amended to exclude IL-2 as an NK cell activating cytokine. Support for the amendments can be found throughout the specification and in the original claims as filed. For example, support for the amendments can be found at paragraphs **[0026]** and **[0030]** of the specification. Likewise, support for the amendment to Claim 8 can be found at, for example, paragraphs **[0035]** and **[0036]** of the specification. No new matter has been added. Claims 1-16 are presented for examination.

Regarding the Claim to Priority

Paragraphs **[0001]** and **[0003]** have been amended to update the status of the priority application and related application, respectively as requested by the PTO. Paragraph **[0001]** now includes the expression "now U.S. Patent No. 6,375,946" since the priority application 09/516,641 has become a patent. Similarly, Paragraph **[0003]** has been updated to reflect the fact that U.S. Application Ser. No. 07/843,052 has issued as U.S. Patent No. 5,348,739.

Regarding the Information Disclosure Statement

The PTO has indicated that some of the references cited in the PTO-1449 were not found with the parent applications and could not be considered. Therefore, the citations were not initialed. For the PTO's convenience, Applicants submit herewith courtesy copies of the references not found with the parent applications. Applicants request that the references be considered by the PTO and that an initialed copy of PTO-Form 1449 be returned to the Applicants. Because the original information disclosure statement and PTO Form-1449 were sent prior to the issuance of a first office action on the merits, it is believed that no fee is required in accordance with 37 C.F.R. § 1.97(b)(3).

Regarding the Double Patenting Rejection under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 1-16 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 11 of U.S. Patent No. 6,071,509[1].

[1] We note that the PTO rejected Claims 1-16 in view of U.S. Patent No. 6,071,501 rather than 6,071,509 but assume that this was a typographical error.

Claims 1-16 were likewise rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 2 and 11 of U.S. Patent No. 6,375,946. Claims 1-8 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,063,373. Finally, claims 1-8 were rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-5 of U.S. Patent No. 6,245,563. Applicants submit herewith a terminal disclaimer, thereby obviating the PTO's rejections based on obviousness-type double patenting.

Claims 1-16 are definite under 35 U.S.C. §112, second paragraph

Claims 1-16 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention. According to the PTO, Claims 1and 8 are indefinite because of the phrase "effective amount." The PTO opines that the claims fail to recite what the amount of NK cell activating cytokine or NK cell activating flavanoid is effective for. Claims 1 and 8 have been amended to recite to clarify that the phrase "effective amount" refers to the amount of NK cell activating cytokine or flavanoid effective for activating NK cells. In view of the foregoing amendments, Applicants submit that the rejection of Claims 1-16 as being indefinite under 35 U.S.C. § 112, second paragraph is rendered moot and should therefore be withdrawn.

Claims 1-16 fully comply with the written description requirement under 35 U.S.C. § 112, first paragraph

Claims 1-16 were rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. According to the PTO, the claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Specifically, the PTO opines that the specification fails to describe the active step of administering to a subject suffering from neoplastic disease an effective amount of an NK cell activating cytokine or an NK cell activating flavonoid because the specification allegedly lacks a description of "effective amounts." Applicants respectfully disagree.

35 U.S.C. §112, first paragraph requires that a specification convey with reasonable clarity to those skilled in the art that the Applicant was in possession of the invention. See *Vas-Cath, Inc. v. Mahurkar,* 935 F.2d 1555, 1563-64 (Fed. Cir. 1991). Applicants submit that the

subject matter of the claims are fully supported by the disclosure of the specification as filed in conformance with the requirements of 35 U.S.C. §112, 1st paragraph.

As detailed above, Claims 1 and 8 have been amended to clarify that the phrase "effective amount" refers to the amount of NK cell activating cytokine or NK cell activating flavonoid effective to activate NK cells. The specification of includes ample guidance with respect to what the appropriate amounts of cytokines or NK cell activating flavonoids are necessary to achieve NK cell activation. In paragraph **[0035]** of the specification, for example, effective amounts of cytokines such as IL-1, IL-2, and IL-12 are set forth. Applicants describe that the effective amount of an NK cell activating cytokine can be between about 1,000 to 300,000 U/kg/day and is more preferably between about 5,000 to 20, 000 U/kg/day. Paragraph **[0036]** details suitable dosage amounts of interferon to achieve tumor growth inhibition. Applicants describe that the effective amount of NK-cell activating interferon is between about 3,000 to 100,000 U/kg/day and is preferably between 10,000 to 50,000 U/kg/day. In paragraph **[0037]** of the specification, the amount of flavonoid for inhibiting tumor growth is described as being between about 1 to about 100,000 mg/day, preferably between about 5 and 10,000 mg/day, and more preferably between about 50 to 1,000 mg/day. Moreover, the Example section of the specification provides numerous examples of combining an NK-cell activating cytokine with a compound effective to inhibit the production or release of hydrogen peroxide. Accordingly, the rejection of the claims under 35 U.S.C. § 112, 1st paragraph should be withdrawn.

CONCLUSIONS

In view of the foregoing amendments and arguments, Applicants respectfully submit that the present application is in condition for allowance. Nevertheless, the PTO is invited to contact the undersigned at the telephone number appearing below to discuss any remaining issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 3 January 2005

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